

# Hepatitis, Infectious, Other

(Including hepatitis D [also known as Delta hepatitis, GD hepatitis, delta associated hepatitis] and hepatitis E [also known as enterically transmitted non-A non-B hepatitis (ET-NANB)])

*NOTE: Hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV) are each covered in a separate chapter in this manual.*



## Section 1:

## ABOUT THE DISEASE

### A. Etiologic Agent

Hepatitis D is caused by the hepatitis D virus (HDV). HDV is a single-stranded RNA virus that contains hepatitis B surface antigen (HBsAg) within its coat. HDV requires the hepatitis B virus (HBV) as a “helper” virus, and it cannot produce infection in the absence of HBV infection.

Hepatitis E is caused by the hepatitis E virus (HEV). HEV is a single-stranded RNA virus. HEV was formerly classified in the Calicivirus family, but has since been distinguished from the caliciviruses.

### B. Clinical Description

HDV infection can occur as an acute co-infection with HBV or as a super-infection in people who are already chronically infected with HBV. The onset of acute co-infection with HDV and HBV is typically abrupt and resembles the signs and symptoms of acute HBV infection, including anorexia, abdominal pain, nausea, vomiting, and jaundice. Acute co-infection is usually self-limited, although the likelihood of fulminant hepatitis can be as high as 5%. When HDV produces a super-infection in those already chronically infected with HBV, it can turn a mild or asymptomatic HBV chronic infection into a severe or fulminant case of hepatitis.

HEV infection ranges from subclinical infection to acute illness, including jaundice, anorexia, fever, abdominal pain, and arthralgia (joint pain). The clinical presentation is similar to that of hepatitis A virus (HAV) infection. HEV infection is usually self-limited, and as with HAV infection, chronic infection does not occur. Pregnant women in the third trimester are particularly vulnerable to fatal complications of HEV infection, and the case-fatality rate can reach 20% in this population.

### C. Vectors and Reservoirs

Humans are the only natural host of HDV. HDV has been transmitted experimentally to some animals (chimpanzees and woodchucks). In endemic areas, HEV infection has been documented in pigs, cattle, and chickens.

### D. Modes of Transmission

HDV can be transmitted through blood or blood products, injection drug use, or sexual contact, as long as HBV is also present in the patient.

HEV is transmitted primarily by the fecal-oral route. The most common vehicle documented during outbreaks is contaminated drinking water. While person-to-person transmission is possible, also through the fecal-oral route, it is believed to occur less commonly with HEV than with HAV. The potential for HEV transmission from contaminated food is still under investigation, and there is no evidence of transmission by percutaneous or sexual exposure. Recent evidence also suggests that HEV infection may be transmitted from infected animals through fecal contamination.

## **E. Incubation Period**

The incubation period for HDV superinfection is about 2–8 weeks. With acute co-infection of HBV and HDV, the incubation period is similar to that of HBV (45–160 days).

The incubation period for HEV ranges from 15–64 days, with a mean of 26–42 days (as seen in prior epidemics).

## **F. Period of Communicability or Infectious Period**

HDV is likely transmissible during all phases of infection. The period of time just prior to the onset of acute illness is likely the most infectious period.

HEV has been detected in stool 14 days after the onset of jaundice and 4 weeks after the ingestion of contaminated food and water. However, the period of communicability for HEV is unknown.

## **G. Epidemiology**

HDV and HEV infections account for a very small percentage of the viral hepatitis cases reported in the U.S.

An estimated ten million people worldwide are co-infected with HDV and HBV. In the U.S., the incidence of HDV cannot be directly calculated from national surveillance data because HDV is not currently nationally reportable. However, in prevalence studies among patients with acute HBV infection, 1.5–7.2% had serologic evidence of HBV-HDV co-infection.

HEV infection is rare in the U.S. Most reported cases are imported from HEV-endemic countries, where contamination of water is common. However, several cases of acute HEV infection have been reported in individuals with no recent travel outside of the U.S. HEV infection should be considered in any patient with non-A, non-B, non-C hepatitis.

## **H. Bioterrorist Potential**

These pathogens are not considered to be of risk for use in bioterrorism.



## Section 2:

# **REPORTING CRITERIA AND LABORATORY TESTING**

## **A. What to Report to the Massachusetts Department of Public Health (MDPH)**

Report any case of clinically-diagnosed hepatitis (with a discrete symptom onset and jaundice or elevated serum aminotransferase [ALT, AST] levels) and the following laboratory findings:

- ◆ Serum aminotransferase levels greater than 2.5 times the upper limit of normal; AND
- ◆ IgM anti-HAV antibody negative; AND

- ◆ IgM anti-HBc antibody negative (if done) or HBsAg negative; AND
- ◆ Anti-HCV antibody negative (if done).

For HDV only:

- ◆ *HDV (Delta hepatitis)*: HBsAg or IgM anti-HBc positive and antibody to hepatitis delta virus positive.

*Note on laboratory testing for HEV: HEV can be diagnosed by detecting IgM antibody to HEV in serum or by detecting HEV RNA by reverse transcriptase-polymerase chain reaction assay in stool or serum specimens. However, such tests are not widely available in commercial laboratories and have not been approved by the Food and Drug Administration (FDA) for diagnostic use. The Centers for Disease Control and Prevention (CDC) recommends testing for HEV when the clinical and laboratory criteria described above have been met.*

## B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) does not provide routine anti-HDV and anti-HEV antibody testing for the general public. Testing is generally conducted through hospital and commercial clinical laboratories.



### Section 3:

## REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

### A. Purpose of Surveillance and Reporting

- ◆ To identify illness clusters or outbreaks as soon as possible.
- ◆ To identify whether the case may be a source of infection for others, and if so, to prevent further transmission.
- ◆ To identify sources of public health concern (e.g., a contaminated water source), and to stop transmission from such sources.
- ◆ To determine the prevalence and etiology of non-A, non-B, non-C hepatitis virus infection in specific populations and geographic locations.

### B. Laboratory and Health Care Provider Reporting Requirements

Infectious hepatitis that is not otherwise specified (as HAV, HBV, or HCV) is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of infectious hepatitis not otherwise specified (as HAV, HBV, or HCV), as defined by the reporting criteria in Section 2A.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of infectious hepatitis infection not otherwise specified (as HAV, HBV, or HCV) shall report such evidence of infection directly to the MDPH within 24 hours.

### C. Local Board of Health (LBOH) Reporting and Follow-up Responsibilities

#### *Reporting Requirements*

MDPH regulations (*105 CMR 300.000*) stipulate that infectious hepatitis not otherwise specified (as HAV, HBV, or HCV) is reportable to the LBOH and that each LBOH must report any case or suspect case of infectious hepatitis

not otherwise specified (as HAV, HBV, or HCV), as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using a MDPH *Generic Confidential Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

### *Case Investigation*

1. It is the responsibility of the LBOH to complete a MDPH *Generic Confidential Case Report Form* (found at the end of this chapter) by interviewing the case and others who may be able to provide information. Much of the information required on the form can be obtained from the health care provider or from the medical record.
2. Use the following guidelines to assist in completing the form:
  - a. Accurately record the demographic information.
  - b. Accurately record clinical information, including “hepatitis, infectious-not otherwise specified” as the disease being investigated, date of symptom onset, symptoms, whether hospitalized, and hospital and clinician contact information.
  - c. Include all available diagnostic laboratory test information.
  - d. Record information relevant to prevention and control. For HEV, use the incubation period range for HEV (15–64 days). Specifically, focus on the period beginning a minimum of 15 days prior to the case's onset date back to no more than 64 days before onset for the following exposures:
    - i. Travel history: Determine the date(s) and geographic area(s) traveled.
    - ii. Contact with another known HEV case.

*Note: With regard to HDV, if the case is a woman of childbearing age (14–44 years of age), clearly indicate whether or not she is pregnant, and if she is, record the estimated delivery date and planned hospital for delivery. (This is important with regard to HBV transmission to and prophylaxis of the newborn.)*
  - e. Include any additional comments regarding the case.
  - f. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.
3. After completing the form, attach laboratory report(s) and fax or mail (in an envelope marked “Confidential”) to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

**MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)**  
**305 South Street, 5<sup>th</sup> Floor**  
**Jamaica Plain, MA 02130**  
**Fax: (617) 983-6813**

4. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.



## Section 4:

# CONTROLLING FURTHER SPREAD

### A. Isolation and Quarantine Requirements (*105 CMR 300.200*)

#### *Minimum Period of Isolation of Patient*

Until documented that illness is not transmissible by the fecal-oral route or until one week after symptom onset, whichever occurs first. Exclusion from organ and blood donation. Case shall receive counseling to modify activities in order to prevent transmission, as appropriate.

#### *Minimum Period of Quarantine of Contacts*

Contacts with diarrhea who are food handling facility employees shall be considered the same as a case and shall be handled in the same fashion. Personal surveillance for high-risk contacts.

### B. Protection of Contacts of a Case

Standard precautions are recommended for HDV cases to prevent exposing others to blood and body fluids. Contact precautions are also recommended for HEV cases.

### C. Managing Special Situations

#### *Reported Incidence Is Higher Than Usual/Outbreak Suspected*

If the number of reported cases of HDV or HEV in your city/town is higher than usual or if you suspect an outbreak, investigate to determine the source of infection and the mode of transmission. Consult with the epidemiologist on-call at the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850. The Division can help determine a course of action to prevent further cases and can perform surveillance for cases across town lines, which would otherwise be difficult to identify at the local level.

#### *Case in a Food Handler or Childcare Provider*

The occurrence of a confirmed case of HEV in a childcare provider or a food handler in Massachusetts would be a highly unusual circumstance. In this situation, the MDPH will work closely with LBOH and will provide instructions/information on how to proceed.

### D. Preventive Measures

#### *HDV*

Since HDV cannot be transmitted in the absence of HBV infection, the prevention of HBV infection through immunization is the best way to prevent HDV infection. For those with chronic HBV infection, the only effective prevention measure is to avoid exposure to any potential source of HDV.

## HEV

Good sanitation and the avoidance of potentially contaminated food and water are the best means to prevent HEV infection. Travelers to areas where HEV is endemic should pay attention to what they eat and drink. Taking precautions, such as those listed below, will help prevent other illnesses as well, including travelers' diarrhea, cholera, dysentery, and typhoid fever.

Recommendations to travelers include:

- ◆ “Boil it, cook it, peel it, or forget it.”
- ◆ Drink only bottled or boiled water, keeping in mind that bottled carbonated water is safer than bottled non-carbonated water.
- ◆ Ask for drinks without ice, unless the ice is made from bottled or boiled water.
- ◆ Avoid popsicles and flavored ices that may have been made with contaminated water.
- ◆ Eat foods that have been thoroughly cooked and are still hot and steaming.
- ◆ Avoid raw vegetables and fruits that cannot be peeled. Vegetables like lettuce are easily contaminated and are very hard to wash well.
- ◆ Peel raw fruits or vegetables, and do not eat the peelings.
- ◆ Avoid foods and beverages from street vendors.

*Note: For more information regarding international travel and HEV, contact the CDC's Traveler's Health Office at (877) 394-8747 or on the CDC website at [www.cdc.gov/travel](http://www.cdc.gov/travel).*



## ADDITIONAL INFORMATION

The formal CDC surveillance case definition for non-A, non-B, non-C viral hepatitis is the same as the criteria outlined in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting. However, non-A, non-B, viral hepatitis has been designated as a nationally, non-notifiable disease since January 1, 2003.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

*Note: The most up-to-date CDC case definitions are available on the CDC website at [www.cdc.gov/epo/dphsi/casedef/case\\_definitions.htm](http://www.cdc.gov/epo/dphsi/casedef/case_definitions.htm).*



## REFERENCES

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## **FORMS & WORKSHEETS**

*Hepatitis, Infectious, Other*



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## LBOH Action Steps

*This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to infectious hepatitis not otherwise specified (as HAV, HBV, or HCV) case investigation activities.*

LBOH staff should follow these steps when infectious hepatitis not otherwise specified (as HAV, HBV, or HCV) is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

- ☐ Notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any suspect or confirmed case(s) of infectious hepatitis not otherwise specified (as HAV, HBV, or HCV).
- ☐ Obtain laboratory confirmation.
- ☐ Fill out the case report form (attach laboratory results).
- ☐ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).

### For HDV

- ☐ If the case is pregnant or has recently given birth, notify the MDPH Immunization Program Perinatal Hepatitis B Nurse, at (617) 983-6800 or (888) 658-2850, as soon as possible.

### For HEV

- ☐ Identify potential exposure sources, such as food or water, and remove any suspect items.
- ☐ For HEV, determine whether the case attends or works at a daycare facility and/or is a food handler.
- ☐ Institute isolation and quarantine requirements (*105 CMR 300.200*), as they apply to a particular case.